Big Pharma and FDA: 
Legal, financial and ideological varieties of corruption

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Combating Corruption in Health Care and Pharmaceuticals

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A Framework for Discussing Corruption


- **Corrupt gain > Penalty × Likelihood of being caught and prosecuted**

If a company (or individual) gains more than loses from corruption, as well as having a low chance of being caught and prosecuted, corruption will more likely flourish.

A modification of this in 2012 by a German scholar, Constantine Stephan, new elements:

- **Degree of corruption = Monopoly + Discretion – Transparency – Morality**

Beyond the original formulation, ethics and financial and other transparencies get into the formula as possible mitigating factors. Independent oversight by non-governmental organizations (NGOs) and the media plus public access to reliable information could reduce the problem.
Why at least two parties (FDA and PhRMA) are needed

• The oft-heard phrase (song) “It takes two to tango”, implies, in this context, that for pharma corruption to flourish, a second party (or more)---the FDA, the legislature or the courts must be complicit.

• Another factor governing the amount of corruption is whether or not it is legal. If illegal, but the penalties are too small, the benefits of corruption to the industry will outweigh these financial or incarceration risks. If legal, the related financial and ideological elements of corruption must be actively involved.
Types of Corruption Adversely Affecting FDA and Public Health

Legislative corruption—laws that benefit industry

Drug industry criminal and civil violations

Corrupt unethical drug industry human experiments

Drug industry-funded meta-analyses to increase marketing

Corrupt advertising to manipulate thinking of doctors (and patients)
## President’s FDA User Fee Budget: FY 2017 for Drugs, Biologics and Devices

<table>
<thead>
<tr>
<th>FDA Center</th>
<th>Total Budget</th>
<th>User Fees</th>
<th>User Fees as % of Total Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drugs</td>
<td>$ 1.41 billion</td>
<td>$0.917 billion</td>
<td>66%</td>
</tr>
<tr>
<td>Biologics</td>
<td>$ 0.360 billion</td>
<td>$0.145 billion</td>
<td>40%</td>
</tr>
<tr>
<td>Devices</td>
<td>$ 0.463 billion</td>
<td>$0.138 billion</td>
<td>30%</td>
</tr>
<tr>
<td>Total of Three centers</td>
<td>$ 2.233</td>
<td>$1.2 billion</td>
<td>54%</td>
</tr>
</tbody>
</table>

Era Of Faster FDA Drug Approval Has Also Seen Increased Black-Box Warnings And Market Withdrawals (Health Affairs July, 2014)

“Drugs approved after the [1992] enactment of PDUFA were significantly more likely to receive a black box warning or withdrawal than drugs approved before PDUFA’s enactment: 26.7 out of 100.0 drugs versus 21.2 out of 100.0 drugs; odds ratio:1.35; p < 0:05) at up to sixteen years of follow-up.”
“Of the 39 new drugs approved in 1997, a fifth (eight) were eventually withdrawn for safety reasons, considerably more than in any year in the 1975 to 2009 interval encompassed by this study. These eight withdrawn drugs were three fluoroquinolone antibiotics, one appetite suppressant, one antidiabetes drug, one statin, one non-steroidal anti-inflammatory drug, and one antihypertensive drug—none arguably breakthrough drugs.”
“In a [Public Citizen] survey of FDA physicians who review drugs conducted in 1998, by which time the PDUFA effect had clearly sunk in

• many of the 53 respondents …thought that standards of safety and efficacy had been weakened

• Nineteen medical officers identified a total of 27 approved new drugs in the past three years that they thought should not have been approved.

• Most of these medical officers said that current FDA standards were “lower” or “much lower” than previous ones.”

Swolfe@citizen.org
Confirmed that decisions concerning drug safety and effectiveness were being overturned. Eighteen percent of surveyed FDA physicians and scientists felt pressure to recommend that drugs be approved for sale despite their reservations about the drug’s safety, efficacy or quality. The report concluded: "Overall, these findings present a significant warning signal."
Recent Examples of Legislative Corruption to Weaken FDA

Beyond the 1992 Prescription Drug User Fee Act (PDUFA) and the evidence just discussed about its damage, there are ongoing legislative efforts to further weaken FDA regulation.

The current scheme, called 21st Century Cures, has passed the U.S. House and is being considered by the Senate. Provisions would:

Bar generic entry of medicines into the market for longer periods

Effectively lower FDA approval standards for antibiotics and antifungals

Undermine the FDA’s ability to ensure the safety and effectiveness of medical devices
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<table>
<thead>
<tr>
<th>Company*</th>
<th>Total Financial Penalties ($ millions)</th>
<th>Percent of Total**</th>
<th>Number of Settlements***</th>
</tr>
</thead>
<tbody>
<tr>
<td>GlaxoSmithKline</td>
<td>$7,881</td>
<td>22.0%</td>
<td>31</td>
</tr>
<tr>
<td>Pfizer</td>
<td>$3,943</td>
<td>11.0%</td>
<td>31</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>$2,824</td>
<td>7.9%</td>
<td>19</td>
</tr>
<tr>
<td>Merck</td>
<td>$1,915</td>
<td>5.4%</td>
<td>30</td>
</tr>
<tr>
<td>Abbott</td>
<td>$1,840</td>
<td>5.1%</td>
<td>16</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>$1,742</td>
<td>4.9%</td>
<td>15</td>
</tr>
<tr>
<td>Teva</td>
<td>$1,471</td>
<td>4.1%</td>
<td>13</td>
</tr>
<tr>
<td>Schering-Plough</td>
<td>$1,339</td>
<td>3.7%</td>
<td>6</td>
</tr>
<tr>
<td>Novartis</td>
<td>$1,250</td>
<td>3.5%</td>
<td>20</td>
</tr>
</tbody>
</table>
Unlawful Promotion ($11,090)
Overcharging Government Health Programs ($5,059)
Financial Violations ($3,562)
Monopoly Practices ($2,121)
Poor Manufacturing Practices ($1,720)
Kickbacks ($743)
Concealing Data ($267)
Environmental Violations ($232)
Illegal Distribution ($67)
Multiple Violations ($10,887)*

Larger financial penalties, especially for repeat offenders, and jail time for executives implicated in criminal activity might actually change the calculus, so that the consequences of lawbreaking are no longer just a cost of doing business for Big Pharma.
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A Drug Company-sponsored Unethical Clinical Trial in Developing Countries

- Discovery Laboratories, Doylestown, PA (Johnson & Johnson Division)

- Synthetic surfactant (Surfaxin)

- 4 surfactants on the market (1st in 1990)

- Associated with 34% relative reduction in neonatal mortality (Cochrane meta-analysis); “Without doubt the most thoroughly studied new therapy in neonatal care” (NEJM review)
A Drug Company-sponsored Unethical Clinical Trial in Developing Countries

- “Further placebo controlled trials of synthetic surfactant are no longer warranted.” (Cochrane)

- FDA: “Conduct of a placebo controlled surfactant trial for premature infants with RDS is considered unethical in the USA.”

- European trial: Surfaxin vs. approved surfactant
42 Randomized Trials of Natural and Synthetic Surfactant in the Treatment of Neonatal Respiratory Distress Syndrome
A Drug Company-sponsored Unethical Clinical Trial in Developing Countries

• Title of internal 2000 FDA meeting: “Use of placebo-controls in life threatening diseases: is the developing world the answer?”

• Location: Mexico, Peru, Bolivia, Ecuador

• Design: Surfaxin vs. placebo (vs. approved surfactant)
A Drug Company-sponsored Unethical Clinical Trial in Developing Countries

- February 2001: Public Citizen writes to HHS Secretary Tommy Thompson urging that these placebo-controlled trials not begin

- March 2001: Bolivian health ministry says the study is “totally prohibited” for legal, ethical and social reasons

- April 2001: Discovery announces study changed to compare to known effective surfactant
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“Only 1,024 and 334 articles published in 1991 were classified as systematic reviews and meta-analyses, respectively. For articles published in 2014, the respective numbers were 28,959 systematic reviews and 9,135 meta-analyses.

This corresponds to an increase in the publication rate of 2,728% for systematic reviews and 2,635% for meta-analyses. When all PubMed-indexed items are considered, 410,093 were published in 1991 and 1,039,145 in 2014, amounting to an increase of only 153% in the publication rate.”
“The production of systematic reviews and meta-analyses has reached epidemic proportions. Possibly, the large majority of produced systematic reviews and meta-analyses are unnecessary, misleading, and/or conflicted.”
(Ioannidis, continued)

Two types of meta-analyses contribute particularly to the multitude of favorable meta-analyses

“The first type is pooled analyses conducted by industry employees…almost all the published articles of this type reached favorable conclusions about the assessed drug.

The second type is meta-analyses where the industry has supported the authors directly (for the particular meta-analysis) or indirectly by promoting their careers in various ways (eg, research grants, speaker bureau membership, paid advisory board positions).”
Further findings in Ioannidis study

• “massive production of redundant meta-analyses of industry products serves as a marketing tool, some sort of petty advertisement, much like seeding randomized trials

• Of 185 [antidepressant] meta-analyses, 54 (29%) had authors who were employees of the assessed drug’s manufacturer, and 147 (79%) had some industry link

• This is a clear example of an area where meta-analyses are emerging as a powerful marketing tool.”
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Advertising:

“the science of arresting the human intelligence long enough to get money from it”

(Definition of advertising by Canadian economist Stephen Leacock in his 1923 book, *The Garden of Folly*)
Ad from ad agency to the marketing departments of drug companies. The McAdam ad agency was owned by owners of Purdue, pushers of Oxycontin.
the hippocampus “processes information by connecting new concepts with the parts of the brain where gut instincts are formed, areas that influence emotional behavior and form memories…… communications are focused on making the [doctor’s] hippocampus respond positively to your product [by demonstrating] how your product is superior and unique”

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39 Public Citizen Petitions to FDA to Ban Prescription Drugs: 1971-2015

- 25 drugs (64%) banned
- 9 drugs (23%) in very limited use
- 5 drugs (13%) still in wide use

Examples: Abbott IV fluids, Darvon, Meridia, Ilosone, phenformin, Oraflex, Suprol, Feldene, Redux, Rezulin, Serzone, Crestor, Bextra, Celebrex